Synthesis of γ-valerolactone using a continuous-flow reactor

József M. Tukacs,[a] Richard V. Jones,[b] Ferenc Darvas,[b] GáborDibó,[a] GáborLezsák,[a] and László T. Mika*[a,c]

[a]Eötvös Loránd University, Institute of Chemistry, Pázmány Péter sétány 1/A, Budapest, H-1117, Hungary
[b]ThalesNano Nanotechnology Inc., H-1031, Budapest, Záhony u.7, Hungary
[c] Budapest University of Technology and Economics, Department of Chemical and Environmental Process Engineering, Budafoki str. 8, Budapest, Hungary, H-1111, Tel: +361463 1263 E-mail: laszlo.t.mika@mail.bme.hu

Electronic Supplementary Information (ESI)

Schematic representation of a continuous-flow reactor: H-Cube® (Ref: 1)

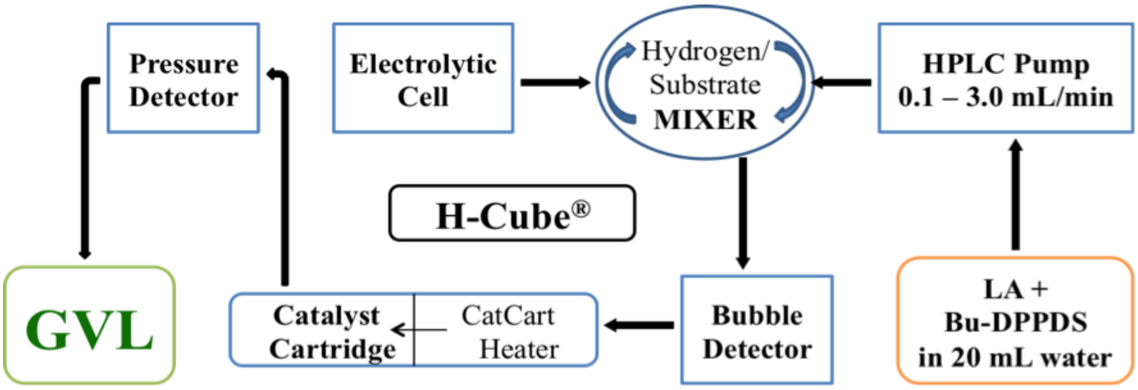
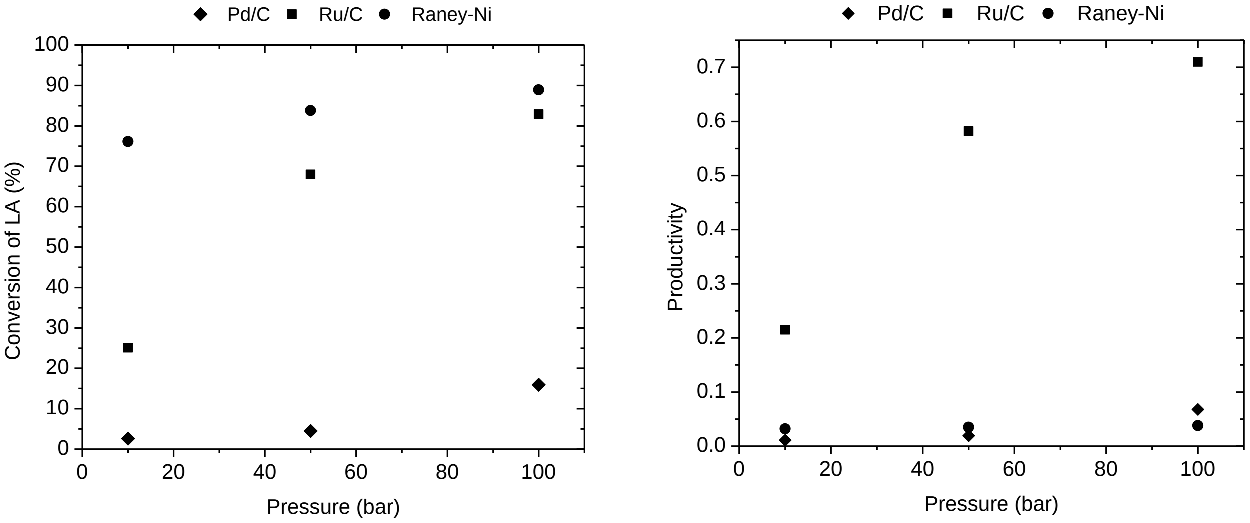


Figure S1. **H-Cube**® hydrogenation system

Table S1. H-Cube® and H-Cube Pro™ reactors for scale-up

Parameters/Advantages[2]	**H-Cube®**	**H-Cube Pro™**
Flow rate range	0.1–3.0 mL/min	0.1–3.0 mL/min
Temperature range	25–100 °C	10–150 °C
Pressure range	1–100 bar	1–100 bar
Concentration range	0.01–0.1 M	0.01–2 M
Capacity of hydrogen production	30 mL/min	60 mL/min
Safety	- no cylinders or other external hydrogen source necessary - no catalyst filtration or direct catalyst handling - easy catalystCatCart® exchange	
Efficiency	analysis of the reaction mixture after 5 min, pressure and temperature can then be adjusted to optimize product conversion to 100%	
Convenience	compact size, fits in a standard laboratory fume hood	



(a) Conversions of levulinic acid to γ-valerolactone in the presence of different catalysts using a flow rate of 1 mL/min at 100 °C. Initial levulinic acid concentration was 0.1 M.

(b) Productivities of the reduction of levulinic acid to γ-valerolactone in the presence of different catalysts using a flowrate of 1 mL/min at 100 °C. Initial levulinic acid concentration was 0.1 M.

Figure S2.

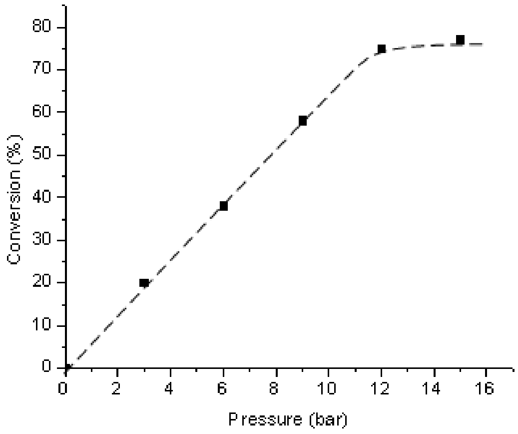
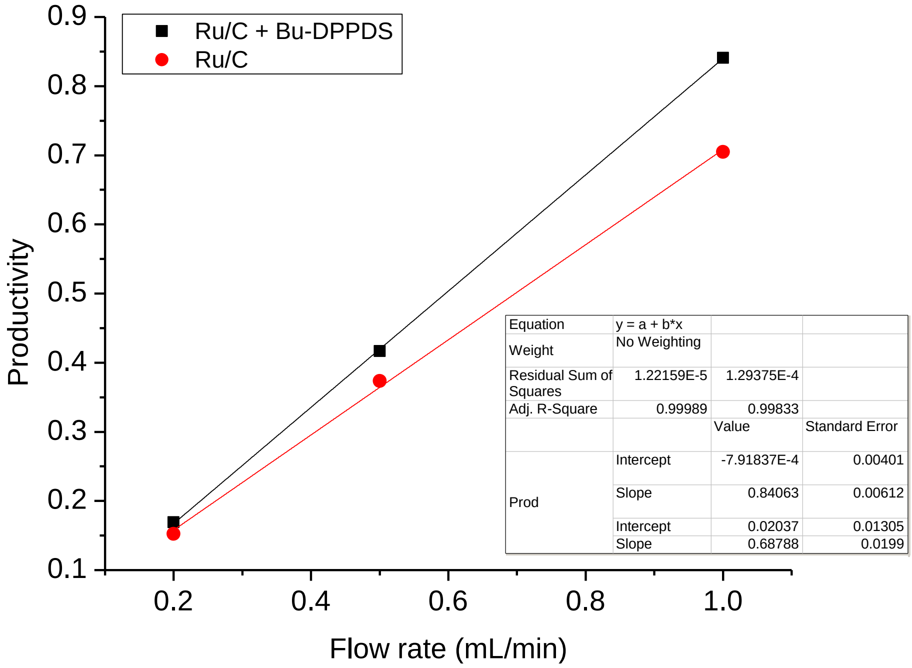


Figure S3. The effect of system pressure on the conversion of LA to GVL
The data are adopted form the paper published by Z. Yan, L. Lin and S. Liu, *Energy & Fuels*, 2009, **23**, 3853.



Flow rate ml/min	Prod. Ru/C + Bu-DPPDS	Prod. Ru/C
0.2	0.1691	0.1522
0.5	0.4167	0.3735
1	0.8409	0.7048

Figure S4. Productivities of GVL as the function of flow rate.

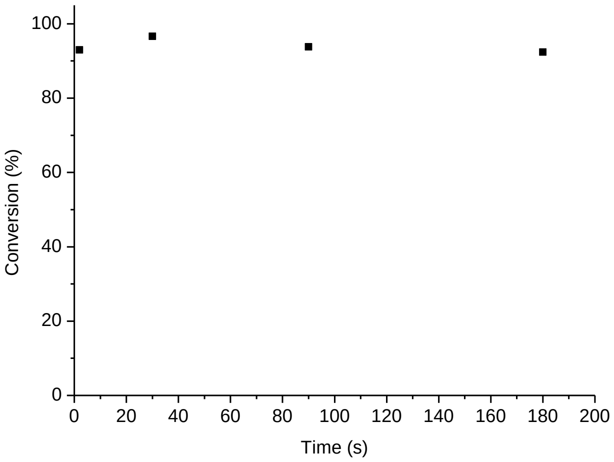


Figure S5. Conversion of LA to GVL.

Conversion of LA to GVL using 5% Ru/C as a catalyst. The selectivity was higher than 99%.

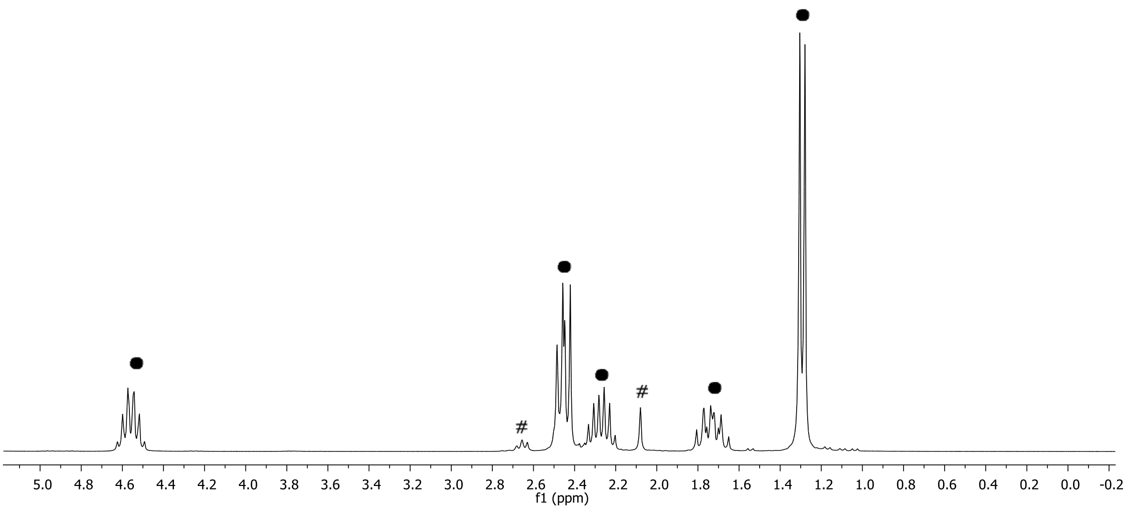


Figure S6. ^{1}H-NMR spectrum of the reaction mixture

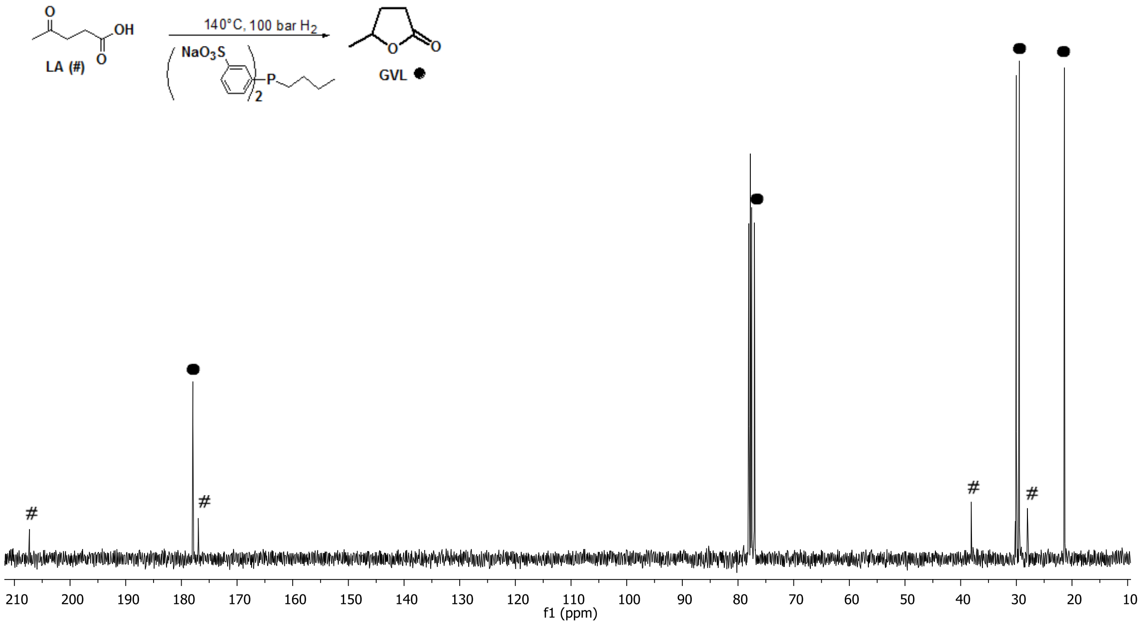


Figure S7. ^{13}C-NMR (in $CDCl_3$) spectrum of the reaction mixture

Table S2. Synthesis of γ-valerolactone using H-Cube® as a continuous-flow reactor system (effect of the flow rate on the conversion) in 20 mL of water under 100 bar of hydrogen at 100 °C

Entry	Catalyst	[Bu-DPPDS] (mmol/L)	**v (mL/min)**	**Conv. (%)**	Productivity ($mol_{GVL} \times g_{Metal}^{-1} \times h^{-1}$)
1	5% Ru/C	-	**0.2**	**88.8**	0.152
2	5% Ru/C	-	**0.5**	**87.2**	0.373
3	5% Ru/C	-	**1.0**	**82.2**	0.704
4	5% Ru/C	-	**1.5**	**71.3**	0.916
5	5% Ru/C	-	**2.0**	**60.9**	1.044
6	5% Ru/C	15	**0.2**	**98.6**	0.169
7	5% Ru/C	15	**0.5**	**97.2**	0.416
8	5% Ru/C	15	**1.0**	**98.1**	0.840
9	5% Ru/C	15	**1.5**	**77.2**	0.992
10	5% Ru/C	15	**2.0**	**65.9**	1.129
11	5% Ru/C	0.15	**1.0**	**95.6**	0.819
12	5% Ru/C	1.5	**1.0**	**98.3**	0.842
13	5% Ru/C	15	**1.0**	**98.5**	0.844
14	Raney-Ni	-	**0.5**	**92.2**	0.019
15	Raney-Ni	-	**1.0**	**88.2**	0.037
16	Raney-Ni	-	**1.5**	**80.1**	0.051
17	Raney-Ni	-	**2.0**	**66.0**	0.056

Table S3. Synthesis of *γ*-valerolactone using H-Cube® as a continuous-flow reactor system (effect of the pressure on the conversion) in 20 mL of water with a flow rate of 1 mL/min at 100 °C

Entry	Catalyst	[Bu-DPPDS] (mol/L)	**p (bar)**	**Conv. (%)**	Productivity ($mol_{GVL}\times g_{Metal}^{-1}\times h^{-1}$)
1	10% Pd/C	-	**10**	**2.6**	0.011
2	10% Pd/C	-	**50**	**4.5**	0.019
3	10% Pd/C	-	**100**	**15.9**	0.068
4	10% Pd/C	0.15	**10**	**3.9**	0.016
5	10% Pd/C	0.15	**50**	**7.7**	0.033
6	10% Pd/C	0.15	**100**	**16.3**	0.069
7	5% Ru/C	-	**10**	**25.1**	0.215
8	5% Ru/C	-	**50**	**68.0**	0.582
9	5% Ru/C	-	**100**	**82.9**	0.710
10	5% Ru/C	0.15	**10**	**39.4**	0.337
11	5% Ru/C	0.15	**50**	**71.8**	0.615
12	5% Ru/C	0.15	**100**	**95.3**	0.816
13	Raney-Ni	-	**10**	**76.1**	0.032
14	Raney-Ni	-	**50**	**83.3**	0.035
15	Raney-Ni	-	**100**	**88.9**	0.038

Table S4. Synthesis of *γ*-valerolactone using H-Cube Pro™ as a continuous-flow reactor system (effect of the pressure on the conversion) in 20 mL of water with a flow rate of 1 mL/min at 140 °C

Entry	Catalyst	[Bu-DPPDS] (mol/L)	**p (bar)**	**Conv. (%)**	Productivity ($mol_{GVL}\times g_{Metal}^{-1}\times h^{-1}$)
1	10% Pd/C	-	**10**	**18.5**	0.079
2	10% Pd/C	-	**50**	**37.7**	0.161
3	10% Pd/C	-	**100**	**44.5**	0.190
4	10% Pd/C	0.15	**10**	**30.9**	0.132
5	10% Pd/C	0.15	**50**	**45.6**	0.195
6	10% Pd/C	0.15	**100**	**51.2**	0.219
7	5% Ru/C	-	**10**	**97.1**	0.832
8	5% Ru/C	0.15	**50**	**98.6**	0.845

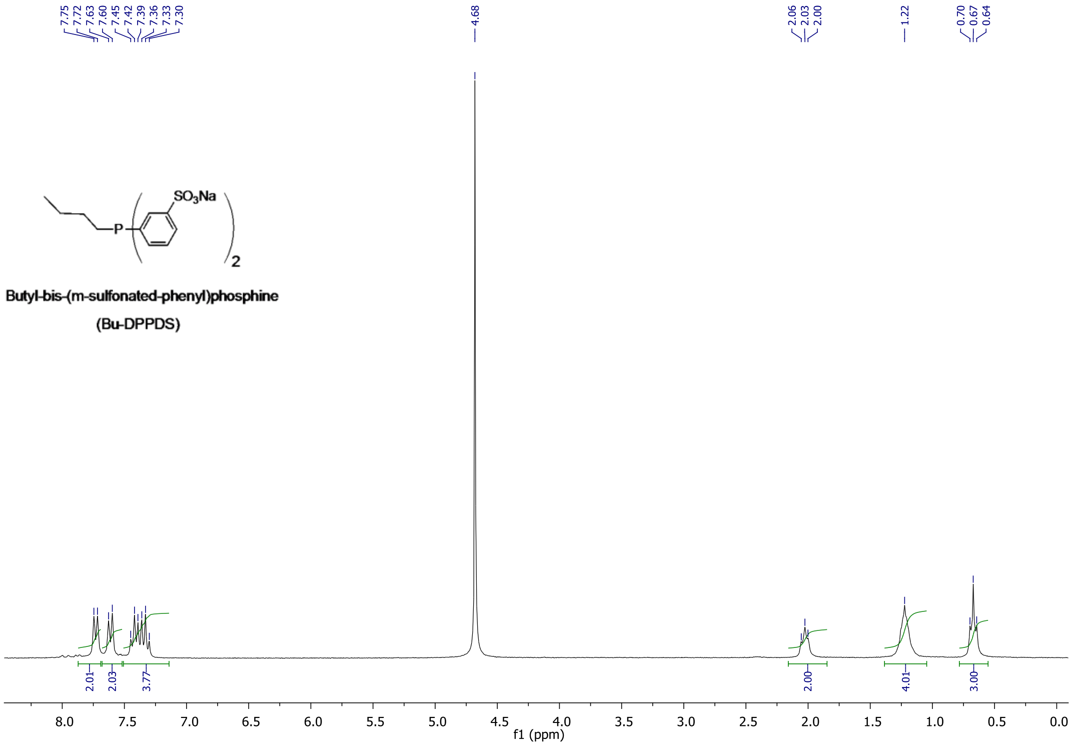
Synthesis of butyldiphenylphosphane[3]

11.5 g (124.6 mmol) butyl chloride in 100 mL diethyl ether was added dropwise to 3.34 g (137.1mmol) magnesium metal pre-activated with a few crystals of iodine, then cooled to 0–5°C and kept under nitrogen. To this solution, 25 g chlorodiphenylphosphane (113.3 mmol) in 100 mL diethyl ether was added through a dropping-funnel with efficient magnetic stirring during 2 hours. The white precipitate was filtered, the filtrate was treated with 3x10 mL water in order to decompose the unreacted Grignard reagent and dissolve the magnesium chloride. The aqueous phase was removed and the organic phase was washed with 2 x 10 mL distilled water. The aqueous phase was discarded. After removing diethyl ether *in vacuo*, butyldiphenylphosphine was obtained as a colorless liquid (21.57 g, yield: 79%).

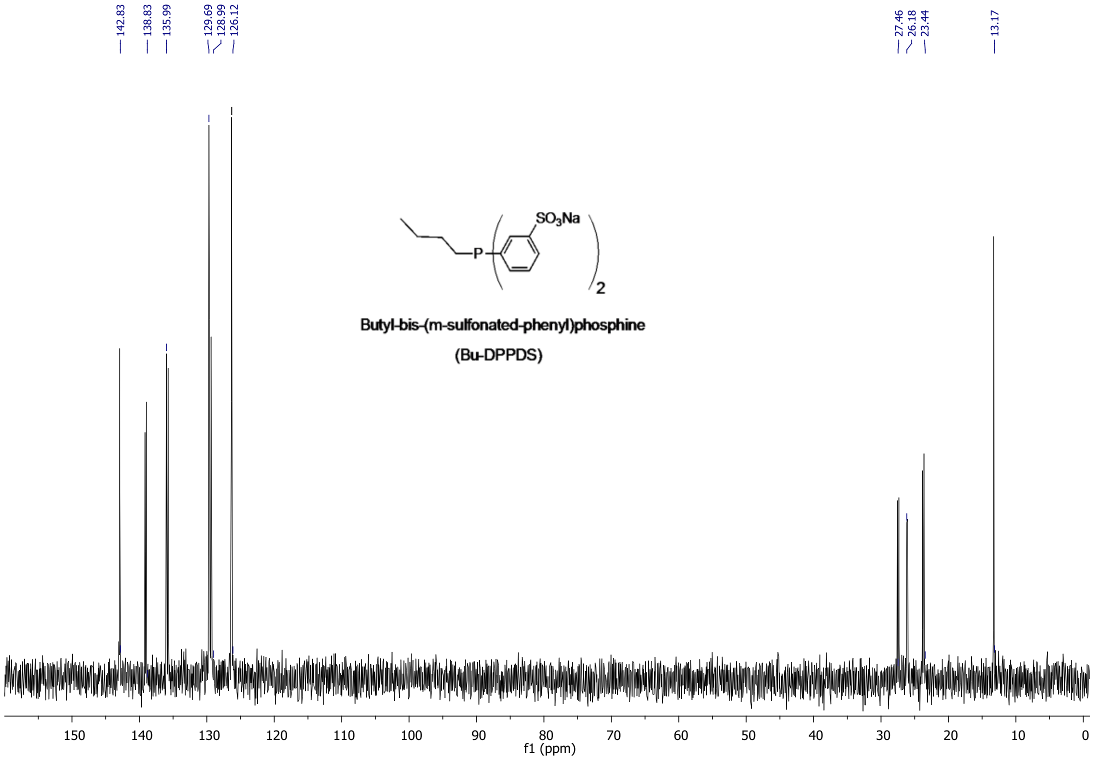
Synthesis of butyl-*bis*(*m*-sulfonatophenyl)phosphane[3] (Bu-DPPDS)

Materials: freshly distilled 5.258g (21.72 mmol) butyldiphenylphosphane, 100 mL of oleum (20%), 50 mL (115.4 mmol) of triisooctylamine, 180 mL toluene. The product (7.14 g) was isolated as white powder. Yield: 73.6%. The purity was checked by ^{31}P-NMR.

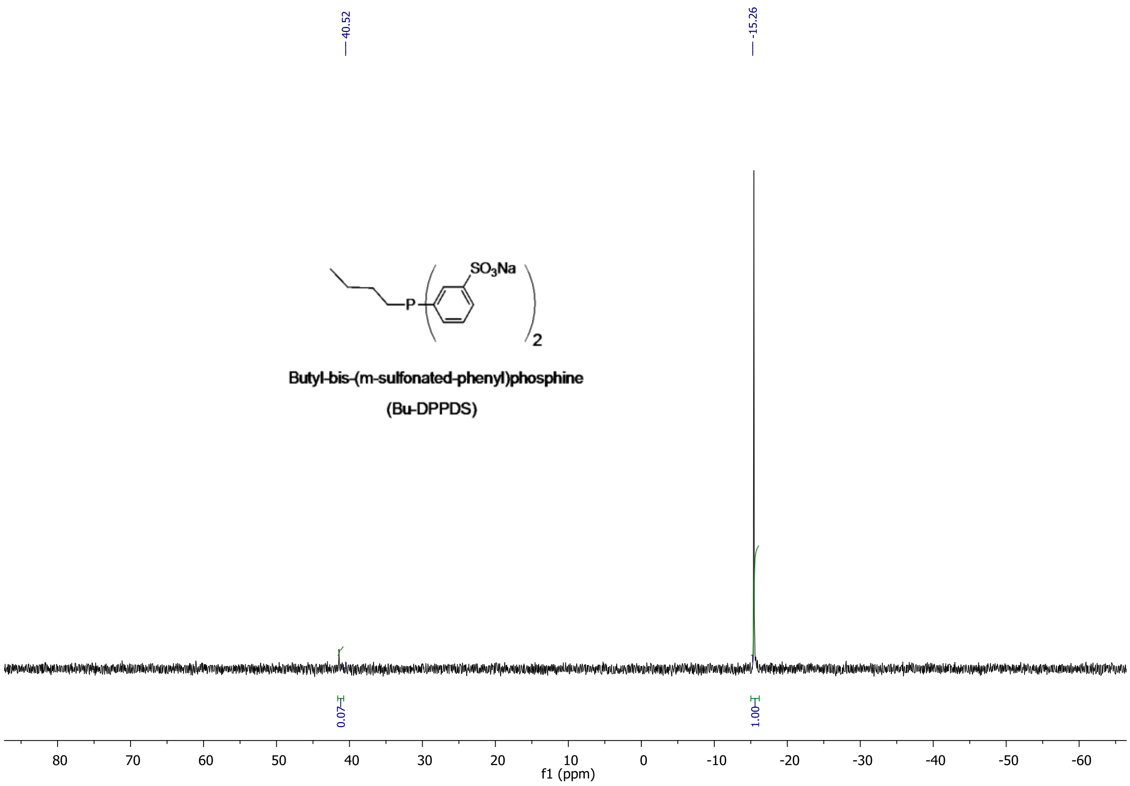
^{1}H–NMR (in D_2O): δ 0.67 (t, 3H, CH_3), 1.22 (m, 4H, 2 CH_2), 2.03 (t, 2H, P–CH_2), 7.3-7.45 (m, 4H), 7.60-7.75 (m, 2+2H). ^{31}P–NMR: δ -15.26 (s). ^{13}C-NMR: δ 13.17 (s), 23.44 (d, $J_{P\text{-}C}$ = 13.8 Hz), 26.18 (d, $J_{P\text{-}C}$ = 7.8 Hz), 27.46 (d, $J_{P\text{-}C}$ = 14.2 Hz), 126.12 (s), 128.99 (d, $J_{P\text{-}C}$ = 10.11 Hz), 129.69 (d, $J_{P\text{-}C}$ = 3.7 Hz), 135.99 (d, $J_{P\text{-}C}$ = 16.55 Hz), 138.83 (d, $J_{P\text{-}C}$ = 11.0 Hz), 142.83 (d, J_{PC} = 6.9 Hz).



^{1}H-NMR spectrum of the Bu-DPPDS



^{13}C-NMR spectrum of Bu-DPPDS



^{31}P-NMR spectrum of Bu-DPPDS.

References

1. B. Desai and O. C. Kappe, *J. Comb. Chem.*, 2005, **7**, 641.

2.http://www.thalesnano.com/products/h-cube

3. L.T. Mika, L. Orha, N. Farkas and I. T. Horváth, *Organometallics*, 2009, **28**, 1593.